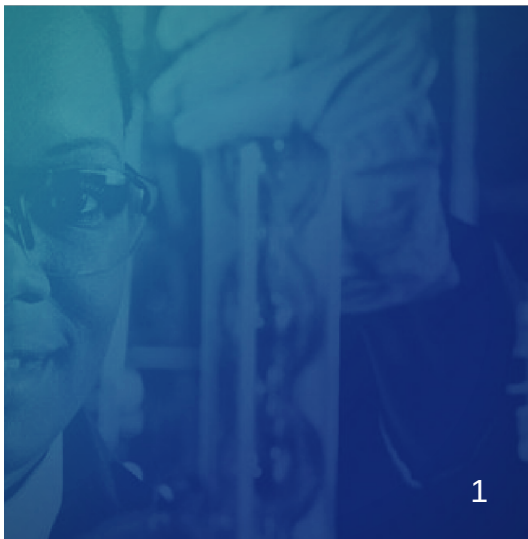
InVivo Biosystems

FUELING DISCOVERY

~Gene By Gene~

InVivo Biosystems provides essential services to help pharmaceutical, nutraceutical, biotechnology companies and academic research institutions worldwide accelerate the discovery and early-stage development of new compounds.

An expert in CRISPR gene editing, InVivo Biosystems creates custom genome-edited *C. elegans* and zebrafish models to enable aging, developmental and other disease studies. Our technologies bridge the gap between cells and mice, providing faster, cost-effective investigations that focus on proof-of-principle experiments for rapid go/no-go decision making.



OVERVIEW OF OUR OFFERINGS

We offer two main services:

1. Genetic Disease Modeling includes Functional Analysis of Variants and Target Identification services
2. Compound Testing includes Compound Efficacy Assessment, Toxicity Testing and Transcriptional Response/RNA-Seq Analysis.

You can learn more about each service and included offerings below.

Functional Analysis of Variants

Conduct pathogenicity assessment of variants in disease related genes.

Our standard process includes:

- Feasibility study of gene(s) for animal modeling. Create and phenotype loss of function knockout mutant lines. Rescue loss of function with expression of human proteins.
- Model known benign and known pathogenic variants. Create and phenotype 5 benign variants and 6 pathogenic variants. Determine the predictive ability of the assay based on the known variants.
- Recommendation of classification of variants based on phenotype(s). Create and phenotype variants of unknown significance and predict pathogenicity.

Target Identification and Validation

Perform expression and knock-out studies to identify and validate drug targets and molecular mechanism of action (MMOA).

Our standard package includes:

- Genetic epistasis studies: Discovery and confirmation of associated genes using overexpression, RNAi knockdown, antisense oligos, and full deletions.
- Gene expression profiling: RNAseq transcriptome analysis, western blotting, fluorescent/ luciferase tagging.
- Full service data pipelines and phenotypic analysis.



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Compound Efficacy Assessment for Anti-Aging Nutritional Supplements

Quickly and economically test a compound's ability to extend lifespan and healthspan with large sample sizes of live animals in less than 5 months and get answers to the following questions:

- Does my compound have a positive or negative effect on lifespan?
- How does my compound affect lifespan AND healthspan?
- Which are the associated signaling pathways that contributed to the life extension?

Choose the package(s) that best suit your needs:

Automated lifespan assay

- High-resolution survival data collected automatically from a large sample size with precision to the hour.
- Assess healthspan by simultaneously collecting movement and morphology data over the entire lifespan of the animals.
- High precision and reproducibility to resolve small changes in lifespan.

Manual lifespan assay

- The gold standard in *C. elegans* longevity assays.
- Ideal for sensitive applications (e.g. requiring supplemental doses, unstable compounds).
- Expert hands-on curation of individual animals for the duration of lifespan.

Longevity package

- Toxicity and Dosage. Dose-response assays to determine ideal dosage and delivery method for the assay.
- Whole transcriptome analysis by RNA-Seq performed in parallel with survival assay to identify potential biological pathways impacted. Includes a longevity-focussed analysis package (as below).

Learn More

OVERVIEW OF OUR OFFERINGS

Toxicity Screening

While we do not suggest replacing mammalian models entirely with *C. elegans* or zebrafish assays for early safety and hazard evaluation, including a small animal model systems such as nematodes or zebrafish can substantially increase predictivity, reducing costs and time through early screening and elimination, and improving prediction of human outcomes.

Our zebrafish toxicity screening includes:

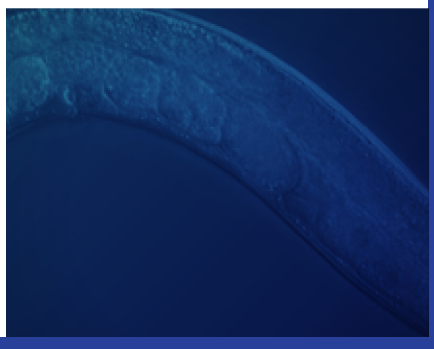
- Acute toxicity & teratogenicity screening: to test acute developmental toxicity studies in zebrafish which can predict mammalian exposure levels associated with embryotoxicity and teratogenicity.
- Molecular Testing: to perform gene expression studies to characterize mechanisms of action.s
- Embryo acute toxicity test: to determine the acute or lethal toxicity of chemicals on embryonic stages of zebrafish.
- Early-life stage toxicity test: to determine the lethal and sub-lethal effects of chemicals on the early life stages of the fish tested.

Our *C. elegans* toxicity screening includes:

- Larval growth assay. Animals are measured during the course of larval development to identify compounds with developmental effects.
- Egg viability assay. Measurement of progeny production is a selective assay to identify compounds likely to be toxic in mammals.
- Molecular Testing. Gene expression studies to characterize mechanisms of action.

Learn More





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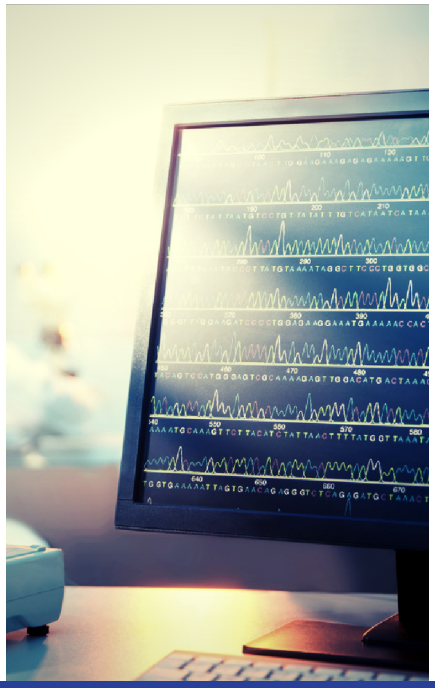
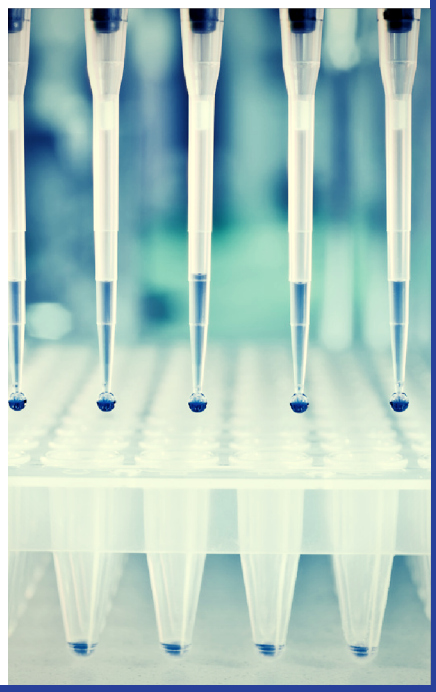
Transcriptional Response/RNA-Seq

To identify potential mechanisms of action for a compound or gene, we analyze global gene expression by RNA-Seq and perform in-depth transcriptional profile and pathway analysis.

Our standard package includes:

- Animal treatment. Animals are grown and exposed to the designated compound or condition and harvested. Total RNA is extracted from the whole animal or specific tissues.
- Sequencing. After RNA sample quality checks, the library is prepared and sequenced. Reads are mapped to the genome for each sample, and additional quality checks are performed on the raw data.
- Bioinformatic Data Analysis. The transcriptome is analyzed to identify genes and pathways that respond to treatment or condition. Analysis includes differential gene expression, volcano plots, heat maps, GO term enrichment, and custom pathway analysis. Raw data, analysis tables, figures, and a summary of findings are delivered to the customer.





ADDITIONAL INFORMATION

Our Approach: Phenotype-based Drug Discovery

Our Phenotype-based Drug Discovery (PDD) method focuses on ameliorating phenotypes to discover efficacious drugs by utilizing powerful small animal models including zebrafish and C. elegans to reduce the cost and speed up the process of identifying lead therapeutics.

This process is particularly well suited for:

- Pre-discovery Stage to understand the disease or condition.
- Target Identification and Validation to select a molecule to target with a drug.

A recent study of approved drugs revealed that Target-based Drug Discovery (TDD), is underperforming relative to Phenotype-based Drug Discovery (PDD). PDD focuses on ameliorating phenotypes to discovery efficacious drugs, whereas TDD focuses on interactions with pre-identified drug targets. Looking broadly back over the past two decades, the PDD approach has resulted in twice as many approved new drugs as TDD[4].

Learn More

Resources:

1. HElio Ortholog Gene Finder: Find a usable model for studying your gene of interest.
2. Disease Gene Finder: Find the link between human disease genes and C. elegans genes and their corresponding phenotypes.
3. Worms on drugs: How well can C. elegans predict drug toxicity in mammals?
4. How Were New Medicines Discovered? Swinney, David C., and Jason Anthony. 2011. Nature Reviews Drug Discovery.

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